

REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-46 were originally filed. In a preliminary amendment, Applicants canceled claims 1-44 without prejudice. Therefore, claims 45-46 were examined on the merits. Claims 45-46 are currently pending. Claims 45 and 46 have been amended. New claims 47-76 are added. No new matter is added. Support for the amendments is supported by the specification.

Claim 45 is amended to recite an enriched $\alpha(2-3)$ sialyllactose formed in a dairy source selected from the group consisting of milk, colostrum and a cheese processing mixture. Support for the amended claim may be found, for example, on page 8, lines 14-15 and page 11, lines 3-5 of the specification. ("The present invention provides a method for producing sialyloligosaccharides in a dairy source...As used herein, "dairy source" includes, but is not limited to milk, colostrum, a cheese processing mixture...").

Claim 45 is also amended to recite the dairy source comprises lactose and sialic acid donors. Support for the amended claim may be found, for example, on page 7, lines 32-36 of the specification. ("More specifically, the method of the present invention uses the catalytic activity of $\alpha(2-3)$ trans-sialidases to exploit the high concentrations of lactose and $\alpha(2-3)$ sialosides which naturally occur in dairy sources, to drive the enzymatic synthesis of $\alpha(2-3)$ sialyllactose.").

Claim 46 is amended to recite an enriched $\alpha(2-3)$ sialyllactose formed in a cheese processing waste stream. Support for the amended claim may be found, for example, on page 8, lines 31-33 of the specification. ("The present invention also provides a method for producing sialyloligosaccharides in a cheese waste stream.").

Claim 46 is amended to recite the cheese processing waste stream comprises lactose and sialic acid donors. Support for the amended claim may be found, for example, on page 7, lines 27-30 of the specification. ("Dairy sources and cheese processing waste streams are known to contain high concentrations of lactose and numerous $\alpha(2-3)$ sialosides, such as, for example, κ casein, and the gangliosides.").

New claim 47 is directed to a Kinetoplastid trans-sialidase. Support for the new claim may be found, for example, on page 12, lines 3-8 of the specification. ("The $\alpha(2-3)$ trans-sialidase used according to the method of the present invention encompasses Kinetoplastid trans-sialidases...").

New claim 48 is directed to $\alpha(2-3)$ trans-sialidase is encoded by a gene isolated from a species of the genera selected from the group consisting of Trypanosoma, Endotrypanum and Pneumocystis. Support for the new claim may be found, for example, on page 12, lines 3-8 of the specification. ("The $\alpha(2-3)$ trans-sialidase used according to the method of the present invention encompasses Kinetoplastid trans-sialidases, trans-sialidases derived from Trypanosoma, Endotrypanum, and Pneumocystis...").

New claim 49 is directed to recombinantly produced $\alpha(2-3)$ trans-sialidase. Support for the new claim may be found, for example, on page 18, lines 22-23 of the specification. ("Recombinant expression techniques can be applied to obtain the $\alpha(2-3)$ trans-sialidases, derivatives, and analogs...").

New claim 50 is directed to the dairy source/trans-sialidase mixture being incubated for at least 1 hour. Support for the new claim may be found, for example, on page 31, lines 24-27 of the specification. ("In specific embodiments, the dairy/trans-sialidase mixture is incubated for a period of at least 0.5, 1.0, 5.0 or 10.0 hours.").

New claim 51 is directed to the cheese processing waste stream/trans-sialidase mixture being incubated for at least 1 hour. Support for the new claim may be found, for example, on page 33, lines 20-23 of the specification. ("In specific embodiments, the waste stream/trans-sialidase mixture is incubated for a period of at least 0.5, 1.0, 5.0 or 10.0 hours.").

New claim 52 is directed to the dairy source/trans-sialidase mixture being incubated at a temperature of about 5° C. to about 45° C. Support for the new claim may be found, for example, on page 32, lines 1-3 of the specification. ("...the dairy/trans-sialidase mixture may be incubated at about 0-45° C, 10-45° C, or 20-40° C.").

New claim 53 is directed to the cheese processing waste stream/trans-sialidase mixture being incubated at a temperature of about 5° C. to about 40° C. Support for the new claim may be found, for example, on page 33, lines 30-32 of the specification. ("In specific

embodiments, the waste-stream/trans-sialidase mixture is incubated at about 2-40° C, preferably 15-37° C, most preferably 22-27° C.”).

New claim 54 is directed to a dairy source/trans-sialidase mixture having a pH of about 6 to about 8. Support for the new claim may be found, for example, on page 32, lines 4-9 of the specification. (“In specific embodiments, the dairy/trans-sialidase mixture is incubated at a pH 5-9, more preferably, at about pH 6-8, and most preferably the pH is at about 7.”).

New claim 55 is directed to a cheese processing waste stream/trans-sialidase mixture having a pH of about 5 to about 8. Support for the new claim may be found, for example, on page 33, line 35-36, and page 34, lines 1-2 of the specification. (“In specific embodiments, the waste stream/trans-sialidase mixture is incubated at a pH 4-9, more preferably, at about pH 6-8, and most preferably the pH is at about 7.”).

New claim 56 is directed to byproducts of cheese manufacturing. Support for the new claim, may be found, for example, on page 11, lines 18-23 of the specification. (“As used herein, “cheese processing waste stream” refers to a byproduct of cheese manufacture and includes, but is not limited to whole whey, demineralized whey permeate, the regeneration stream from demineralized whey permeate, whey permeate, crystallized lactose, spray dried lactose, whey powder, edible lactose and lactose.”).

New claims 57 and 58 are directed to recovering $\alpha(2-3)$ sialyllactose. Support for the new claims may be found, for example, on page 34, lines 24-30 and page 35, lines 1-5 of the specification. (“Sialyloligosaccharides produced according to the methods of the present invention may be recovered from the dairy source before or during processing...In specific embodiments of the invention, $\alpha(2-3)$ sialyloligosaccharides produced according to the methods of the invention, are recovered from a cheese processing stream...”).

New claims 60 and 61 are directed to ultrafiltration. Support for the new claims may be found, for example, on page 36, lines 30-35 of the specification. (“In another embodiment of the invention, sialyloligosaccharides produced according to the methods of the invention are recovered from a dairy source or cheese processing waste stream by a method comprising: subjecting a dairy source or cheese processing waste stream to ultrafiltration...”).

New claims 61 and 62 are directed to contacting the ultrafiltrate with an ion exchange resin. Support for the new claims may be found, for example, on page 49, lines 34-37 of the specification. ("In order for milk whey proteins such as beta-lactoglobulin to be efficiently adsorbed to a cation exchanger, the dairy source or whey may be previously concentrated with an ultrafiltration device.").

New claims 63 and 64 are directed to an anion exchange resin. Support for the new claims may be found, for example, on page 37, lines 32-35 of the specification. ("In a preferred embodiment, the sialyloligosacchides produced according to the methods of the invention are recovered from a dairy source or cheese processing waste stream utilizing an anion exchange resin.").

New claims 65 and 66 are directed to a cation exchange resin. Support for the new claims may be found, for example, on page 39, lines 1-2 of the specification. ("The dairy source or cheese processing waste stream can be contacted with the cation exchange resin...").

New claim 67 is directed to recovering the $\alpha(2-3)$ sialyllactose from a dairy source/trans-sialidase mixture using a solvent. Support for the new claim may be found, for example, on page 46, lines 28-page 49, line 3 of the specification. ("According to this embodiment, a dairy source or cheese processing waste stream is contacted with a solvent, wherein sialyloligosacchides are extracted...").

New claim 68 is directed to recovering the $\alpha(2-3)$ sialyllactose from a cheese processing waste stream/trans-sialidase mixture using a solvent. Support for the new claim may be found, for example, on page 46, line 28-page 49, line 3 of the specification. . ("According to this embodiment, a dairy source or cheese processing waste stream is contacted with a solvent, wherein sialyloligosacchides are extracted...").

New claim 69 is directed to a solvent being selected from water and C_1-C_5 alcohols. Support for the new claim may be found, for example, on page 47, line 35 of the specification. ("Suitable solvent systems are water, $C[1-5]$ alcohols...").

New claim 70 is directed to the mother liquor being obtained by crystallizing lactose from whey. Support for the new claim may be found, for example, on page 11, lines 35-

36 and page 12, line 1 of the specification. ("Whey permeate can be further processed by crystallizing lactose to form both lactose and a mother liquor.").

New claim 71 is directed to exogenous $\alpha(2-3)$ sialyloligosaccharides being added during the incubation step. Support for the new claim may be found, for example, on page 34, lines 10-12 of the specification. ("In one embodiment of the invention, exogenous $\alpha(2-3)$ sialyloligosaccharides are added to dairy source/trans-sialidase mixture.").

New claim 72 is directed to processing the dairy source/trans-sialidase mixture for cheesemaking before the recovery step. Support for the new claim may be found, for example, on page 32, lines 36-37-page 33, line 1 of the specification. ("Where the dairy/trans-sialidase mixture is to be used to manufacture cheese, the dairy/trans-sialidase mixture is collected and processed for making cheese.").

New claim 73 is directed to different types of lactose. Support for the new claim may be found, for example, on page 11, lines 18-23 of the specification. ("As used herein, "cheese processing waste stream" refers to a byproduct of cheese manufacture and includes, but is not limited to whole whey, demineralized whey permeate, the regeneration stream from demineralized whey permeate, whey permeate, crystallized lactose, spray dried lactose, whey powder, edible lactose and lactose.").

New claim 74 is directed to $\alpha(2-3)$ sialosides. Support for the new claim may be found, for example, on page 7, lines 27-30 of the specification. ("Dairy sources and cheese processing waste streams are known to contain high concentrations of lactose and numerous $\alpha(2-3)$ sialosides, such as, for example, κ casein, and the gangliosides.").

New claim 75 is directed to κ casein, and the gangliosides. Support for the new claim may be found, for example, on page 7, lines 27-30 of the specification. ("Dairy sources and cheese processing waste streams are known to contain high concentrations of lactose and numerous $\alpha(2-3)$ sialosides, such as, for example, κ casein, and the gangliosides.").

New claim 76 is directed to sialyl- $\alpha(2-3)$ - β -galactosides. Support for the new claim may be found, for example, on page 3, lines 7-8 of the specification. ("In mammalian cells, sialic acids are most frequently linked to β -galactose with an $\alpha(2-3)$ linkage...").

II. The Invention

The invention includes processes for producing sialyloligosaccharides in a dairy source and a cheese processing waste stream.

III. Responses to the Rejections

Under 35 U.S.C. 102(b)

To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is either expressly found or is inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. See MPEP § 2131. Applicants submit that each element of the claims now pending has not been identified in the art presently of record. Therefore, Applicants traverse the following rejection.

Over Vandekerckhove

Claims 45 and 46 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Vandekerckhove *et al.* ("Substrate Specificity of the *Trypanosoma cruzi* trans-sialidase," *Glycobiology*, **2(6)**, 541-548 (1992))("Vandekerckhove"). Specifically, the Examiner states that Vandekerckhove discloses the preparation of $\alpha(2-3)$ sialyllactose by contacting lactose with $\alpha(2-3)$ trans-sialidase from *Trypanosoma cruzi* in the presence of various oligosaccharides. However, Applicants submit that Vandekerckhove is missing at least four elements which are present in Applicants' invention as claimed.

First, Applicants have amended claim 45 to recite that an enriched $\alpha(2-3)$ sialyllactose is formed in a dairy source selected from the group consisting of milk, colostrum and a cheese processing mixture. In contrast, Vandekerckhove fails to teach that $\alpha(2-3)$ sialyllactose is formed in a dairy source selected from the group consisting of milk, colostrum and a cheese processing mixture.

Second, Applicants have amended claim 46 to recite that an enriched $\alpha(2-3)$ sialyllactose is formed in a cheese processing waste stream. In contrast, Vandekerckhove fails to teach that $\alpha(2-3)$ sialyllactose is formed in a cheese processing waste stream.

Third, Applicants have clarified that the dairy source in claim 45 comprises both the lactose and sialic acid donors. Similarly, Applicants have also clarified that the cheese processing waste stream in claim 46 comprises both the lactose and sialic acid donors. In contrast, Vandekerckhove discloses that the lactose and sialic acid donors are obtained from two separate sources. See "Enzyme activity measurements" on page 547 of Vandekerckhove. Since lactose and the sialic acid donors are obtained from two separate sources, it further supports Applicants' assertion that the reactions in Vandekerckhove do not occur in a dairy source or a cheese processing waste stream.

As set forth above, since Vandekerckhove is missing at least four elements of Applicants' claimed invention, an anticipation rejection cannot be maintained.

Therefore, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-442-1000.

Respectfully submitted,



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